AMERICAN
SOCIETY FOR
MICROBIOLOGY

*Public and Scientific Affairs Board*



April 6, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

RE: Discussion Paper: "A Proposed Framework for Evaluating and Assuring the Human Safety of the Microbial Effects of Antimicrobial New Animal Drugs Intended for Use in Food-Producing Animals." Food and Drug Administration (FDA), Department of Health and Human Services (HHS)

Docket No. 98D—1146

The following comments and recommendations from the American Society for Microbiology (ASM) pertain to the FDA discussion paper, "A Proposed Framework for Evaluating and Assuring the Human Safety of the Microbial Effects of Antimicrobial New Animal Drugs Intended for Use in Food-Producing Animals" [*Federal Register*, January 6, 1999, 64: 887-888]. The 42,000-plus membership of ASM, which is deeply concerned about the complex issue of antibiotic resistance and in ensuring the continued effectiveness of antimicrobial drugs, brings many kinds of expertise to this multifaceted public health challenge.

In its 1994 Report, the ASM Task Force on Antibiotic Resistance stated that there is an urgent need for more prudent use of antibiotics in both human and veterinary medicine, particularly as it relates to food production. The report also emphasized that there is a need to strengthen the curriculum of human and veterinarian health care professionals in the areas of sterilization and disinfection, mechanisms of antibiotic resistance and factors contributing to its spread, including inappropriate antibiotic usage. The ASM strongly recommended, and continues to recommend, that federal funding be allocated for national surveillance of antibiotic resistant bacteria in animals, humans and food products and for the development of new antimicrobials, vaccines and other preventative measures, including education campaigns directed at health professionals, patients and food producers to reduce inappropriate uses of antibiotics.

The ASM commends FDA officials in the Center for Veterinary Medicine for their efforts to address within the new animal drug approval process the human health risks of antibiotic resistance in foodborne pathogens and the relationship of these risks to the use of antimicrobial drugs in food-producing animals. The ASM also acknowledges the ongoing need for

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veterinarians to prevent and treat diseases in food animals and to have appropriate antibiotics available for this important purpose.

The ASM believes that the components outlined in the FDA framework for risk categorization are based on sound general principles. Although the challenges entailed in implementing the principles will require careful and extensive consideration, such practical uncertainties should neither forestall nor reduce efforts to move this deliberative process forward.

ASM recognizes the complexities involved in assessing antibiotic resistance thresholds, establishing monitoring requirements, and taking other measures necessary for implementing the FDA framework. Hence, ASM urges agency officials to convene a series of small working groups, whose participants would provide expertise on appropriate animal and human health issues relating to antibiotic use and resistance, to assess approaches that come within the FDA framework proposal and to develop specific recommendations for agency officials to consider when translating the framework principles into practice.

In addition to this general recommendation to establish a series of expert working groups, ASM also has a number of specific comments and suggestions regarding the FDA Framework.

First, the ASM believes that monitoring of antibiotic resistance is essential to the effectiveness of the proposed program and the results of such monitoring efforts should be subject to regular reviews. The ASM Task Force specifically recommended establishing a national surveillance system under the National Center for Infectious Diseases of the Centers for Disease Control and Prevention. This monitoring effort remains critical for the proposed FDA Framework objectives in order to document, on a continual basis, changes in trends of antimicrobial susceptibility of both human and animal microbial isolates. Although data based on measuring the antibiotic susceptibility of animal-associated microorganisms may be more sensitive, (particularly for those bacteria common to both animals and people), data based on human-associated microorganisms are likely to be more specific for the purpose of assessing resistance trends with the greatest impact on human health. Consistent with the concept featured in the 1994 Task Force report , the ASM recommends strengthening and enhancing the ongoing National Antibiotic Resistance Monitoring Program (NARMS) that tests isolates of specific microorganisms, including *Salmonella*, *Escherichia coli*, and *Campylobacter jejuni*, obtained from humans, animals, and animal carcasses.

Second, ASM further recommends that FDA explore the establishment of programs for collecting information potentially useful for correlating antibiotic use and resistance patterns. Information such as the amounts of antibiotic administered to food animals, the intended uses, the route and the duration of use would be useful. Also, fates of those drugs in the farm environment would be a further area of exploration. The value and practical feasibility of such information gathering programs, including on-farm monitoring projects, should be carefully evaluated by expert working groups before being established.

Third, the ASM recommends that FDA review the three-tiered system for categorizing antimicrobial drugs that is described in its discussion paper. While Category I seems to be clear, Category II is ill-defined and Category III may include uses of drugs which still pose problems to

human health, depending on whether the drug entity is known and already dismissed for human use or is not known and could eventually be used in humans. Moreover, because the duration of exposure to an antibiotic is a critical factor affecting the development of resistance to individual drugs and of multidrug resistance, agency officials will need to develop approaches for dealing with such complex factors within this new framework.

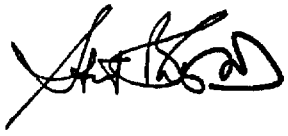
Fourth, the ASM wants to remind FDA officials to avail themselves of findings and recommendations from other groups in the United States and abroad that have dealt with the broad issue of antibiotic resistance. FDA officials should review additional recommendations outlined in the 1994 ASM Task Force report as well as in other reports on this subject from the National Research Council, the Institute of Medicine, the U.S. Office of Technology Assessment, and in the Judicious Use Guidelines in Veterinary Medicine. Much of the information outlined in those reports addresses issues that are described in the agency framework document. In addition, the agency should carefully evaluate the recommendations from the World Health Organization (Berlin, 1997), in particular that which proposes the progressive removal of the use of antibiotics as growth promoters. Since the European Commission has recently invoked the Precautionary Principle to suspend the use of certain antibiotics in animal feeds for growth promotion, in the United States the application of the Framework concepts would offer a consistent scientific approach worldwide.

Fifth, FDA officials need to balance their responsibility for protecting public health with issuing new regulations that are workable for all the parties affected by them, including food producers, veterinary practitioners, and the veterinary pharmaceutical industry. These regulations should be retroactive to include all current antibiotic usages as well as future uses.

Finally, it is essential that FDA continue to conduct relevant research and have adequate resources and appropriately trained personnel, needed for dealing with the complex issue of antibiotic resistance; as well as sufficient reviewers to complete the timely approval of new products, including non-antibiotic alternatives, to be used in food animals.

We appreciate the opportunity to comment on this important document. The ASM would be pleased to assist the FDA in any way possible.

Sincerely,



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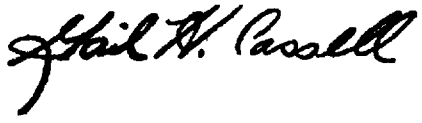

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